Remarks

Reconsideration of this Application and entry of the foregoing amendments are respectfully requested. Firstly, Applicants confirm the election of Group I (claims 1-6 and 9-12). Applicants timely filed a Reply to Restriction Requirement on January 25, 2002, with Petition for Extension of Time, electing Group I in response to a Restriction Requirement mailed on November 27, 2001. Thus, Applicants submit herewith copies of the Reply to Restriction Requirement and PTO date stamped return postcard as evidence of filing.

Upon entry of the foregoing amendments, claims 1-6, 9-12 and 24-27 are pending in the application, with claims 1, 6 and 27 as being the independent claims. Claims 7-8 and 13-23 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein. New claims 24-27 are sought to be added. Support for the amendments to the claims may be found throughout the specification as originally filed. Further support for the amendments to claims 1, 3, 6 and new claims 24 and 27 can be found, for example, at page 7, at lines 12 to 16 and in SEQ ID NOs 1 and 2, showing in SEQ ID NO:1 the long sequence, containing the additional sequence and SEQ ID NO: 2, showing the short sequence (or prostate cancer-associated sequence). Further support for the amendment to claim 3 as it relates to the hybridization can be found, for example, from page 12, line 26 to page 13, line 17. Further support for claim 5 can be found, for example, in SEQ ID NO: 3, which shows a truncated PCA3 protein (the full-length protein having a sequence of fifty-one amino acids), as well as, for example, at page 8, starting at line 27 to page 9, line 8. New claim 25 is identical to claim 2 except for its dependency. Further support for new claim 27 can be found, for example, in claim 3 which more specifically relates to a nucleic acid sequence which is found in the long mRNA described in SEQ ID NO: 1 and absent in

SEQ ID NO: 2. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding rejections and that they be withdrawn.

Rejection under 35 U.S.C. § 112, Second Paragraph

In the Office Action at page 3, the Examiner has rejected claims 1, 3 and 6 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse this rejection.

The Examiner states that "[i]t is indefinite in claims 1 and 6 as to the metes and bounds of 'long.' There is no clear indication as to what constitutes a 'long' sequence." Office Action at page 3. Solely to advance prosecution and not in acquiescence of the Examiner's rejection, Applicants have amended the claims 1 and 6 to recite that the molecule is longer than the sequence set forth in SEQ ID NO:2, or recites the interrupting sequence (nucleotides 27-254 in SEQ ID NO:1), respectively.

Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Rejection under 35 U.S.C. § 112, First Paragraph

In the Office Action at pages 4-5, the Examiner has rejected claims 3 and 6 under 35 U.S.C. § 112, first paragraph, as allegedly non-enabled. Applicants respectfully traverse this rejection.

While the Examiner states that the specification is enabling for an isolated nucleic

acid comprising SEQ ID NO:1, 3, and 4, or a full complement thereof, the Examiner further states that the specification is not enabled for a nucleic acid molecule at least 90% identical to SEQ ID NO:1, and 3, and a complement thereof or a nucleic acid sequence that is complementary to at least 10 nucleotides of SEQ ID NO: 4. *See* Office Action at page 4. Applicants respectfully disagree. The Examiner's argument for lack of enablement in large part is based on the fact that:

> the specification does not give any guidance to which molecules having at least 90% sequence identity to SEQ ID NO:1 and 3, or a complement thereof and a sequence that is complementary to at least 10 nucleotides of SEQ ID NO: 4, *will exhibit the biological activities claimed, or any guidance as to which region of the sequence must be preserved so that the molecule will function as claimed.*

Office Action at page 4 (emphasis added). Applicants respectfully disagree. By the foregoing amendments, claims 3 and 6 recite the additional sequence between exon 3 and exon 4a. Furthermore, the reference to SEQ ID NO:4, previously found in claim 6, has been deleted. In addition, Applicants respectfully submit that in view of the fact that the sequence present in the long mRNA (SEQ ID NO:1) and absent in the short (SEQ ID NO:2) interrupts or destroys the cancerous function of the *short* sequence, that the retention of the biological activity hurdle is much easier to satisfy. Indeed, Applicants respectfully submit that a person of ordinary skill in the art, cognizant of the present invention and more particularly of page 8, line 27 to page 9 line 8, could without undue experimentation assess the phenotype associated with an interruption of the short PCA3 sequence (thereby yielding a longer sequence). It is respectfully submitted that since the interruption of the sequence can be viewed as engendering a loss of function, the fact that:

> even a single amino acid substitution or what appears to be an inconsequential chemical modification will often dramatically affect the biological activity and characteristic of a protein.

actually supports the Applicants' contention, that the specification is enabling for a sequence which interrupts the short PCA3 sequence defined in SEQ ID NO:2. Office Action at page 5.

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph are respectfully requested.

Rejection under 35 U.S.C. § 102

In the Office Action at pages 5-6, the Examiner has rejected claims 1-3, 5 and 9-12 under 35 U.S.C. § 102(e) as being anticipated by Bussemakers, WO 98/45420 A1 (1998) (Doc. AL1 of record; hereinafter "Bussemakers"). Applicants respectfully traverse this rejection.

The Examiner states that "Bussemakers disclose the PCA3 antigen as set forth in SEQ ID NO:3." Office Action at page 6. The Examiner further alleges that "Bussemakers disclose a complement to SEQ ID NO:4 as probes and primers are used in the detection of PCA3 molecules." *Id.* Applicants respectfully disagree. Applicants respectfully submit that Bussemakers does not teach or suggest: (1) the long PCA3 sequence (SEQ ID NO:1) or the sequence spanning nucleotides 27-254 of SEQ ID NO:1; (2) that the short and long sequences of PCA3 can be linked to a cancer or normal phenotype, respectively; and (3) that the additional sequence of SEQ ID NO:1, interrupts the PCA3 open reading frame, thereby truncating same (as set forth in SEQ ID NO:3). Thus, since Bussemakers does not teach the nucleotide sequence set forth from nucleotides 27 to 254 of SEQ ID NO:1, it cannot teach SEQ ID NO:4 which is an example of an oligonucleotide which specifically hybridizes to a subset of the sequence spanning from nucleotides 27 to 254 of SEQ ID NO:1 (i.e. nucleotides 92 to 111 of SEQ ID NO:1).

Accordingly, reconsideration and withdrawal of the rejection under 35 U.S.C. §102(e) is respectfully requested.

Conclusion

All of the stated grounds of rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Angelique G. Uy
Agent for Applicants
Registration No. 48,832

Date: 07/11/2002

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

Version with markings to show changes made

(a) New claims 24-27 are added.

(b) Claims 1, 3, 5 and 6 are amended as follows:

1. (Once Amended) An isolated nucleic acid molecule encoding a differentially expressed prostate cancer antigen 3 (PCA3) mRNA containing an additional sequence between exon 3 and exon 4a, thereby giving rise to a [long] PCA3 mRNA, having a sequence which is longer than that set forth in SEQ ID NO:2.

3. (Once Amended) The isolated nucleic acid molecule according to claim 1, comprising a polynucleotide sequence at least 90% identical to a sequence selected from the group consisting of:

(a) a nucleotide sequence as set forth [in] from nucleotides 27 to 254 of SEQ ID NO:1;

(b) a nucleotide sequence [encoding a differentially expressed PCA3 polypeptide comprising the complete amino acid sequence in SEQ ID NO:3] fully complementary to the nucleotide sequence in (a); and

(c) a nucleotide sequence [complementary] which hybridizes under high stringency condition to any of the nucleotide sequences in (a) or (b).

5. (Once Amended) The isolated nucleic acid molecule according to claim 1, wherein the molecule encodes [the polypeptide comprising the complete] the truncated PCA3 protein having the amino acid sequence set forth in SEQ ID NO:3.

6. (Once Amended) An isolated nucleic acid molecule consisting of 10 to 50 nucleotides which specifically hybridizes to a differentially expressed [long] PCA3 mRNA comprising an additional PCA3 sequence between exon 3 and exon 4a, thereby giving rise to a PCA3 mRNA having a sequence which is longer than that set forth in SEQ ID NO:2, wherein said nucleic acid molecule is or is complementary to a nucleotide sequence consisting of at least 10 consecutive nucleotides from said additional PCA3 sequence, as set forth [in SEQ ID NO:4] from nucleotides 27 to 254 of SEQ ID NO:1.